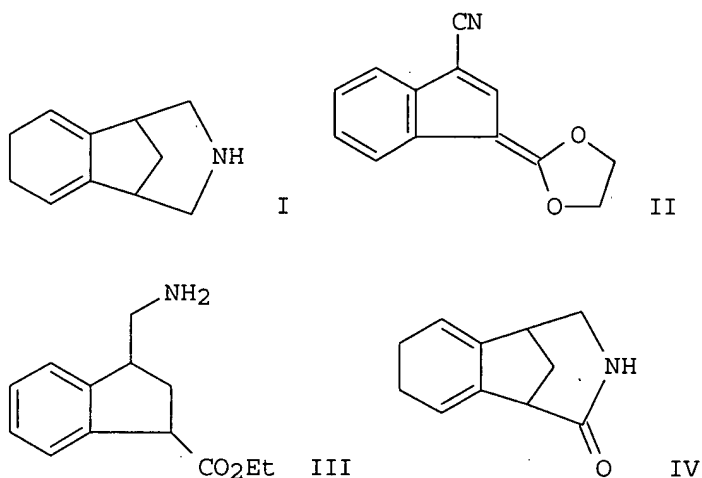


4/14/05

ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2004:462904 CAPLUS
 DOCUMENT NUMBER: 141:190669
 TITLE: Preparation of 1,5-Methano-2,3,4,5-tetrahydro-1H-3-benzazepine via Pd-Catalyzed Cyclization
 AUTHOR(S): Singer, Robert A.; McKinley, Jason D.; Barbe, Guillaume; Farlow, Robin A.
 CORPORATE SOURCE: Chemical Research and Development, Pfizer Global Research and Development, Pfizer Inc., Groton, CT, 06340, USA
 SOURCE: Organic Letters (2004), 6(14), 2357-2360
 CODEN: ORLEF7; ISSN: 1523-7060
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 141:190669
 GI



AB A new approach to prepare 1,5-methano-2,3,4,5-tetrahydro-1H-3-benzazepine (I) is discussed. This strategy utilized a tandem Michael addition and Pd-catalyzed cyclization to afford cyanobenzofulvene acetal II. This indene intermediate (II) was subjected to hydrogenolysis to provide an amino ester (III) and was cyclized with base to afford lactam IV. The lactam (IV) was reduced with borane to afford the desired benzazepine (I).

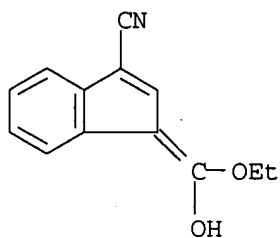
IT **474024-31-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 1,5-methano-2,3,4,5-tetrahydro-1H-3-benzazepine via tandem Michael addition and Pd-catalyzed indene cyclization, hydrogenolysis, lactam cyclization, and reduction)

RN 474024-31-2 CAPLUS

CN 1H-Indene-3-carbonitrile, 1-(ethoxyhydroxymethylene)-, sodium salt (9CI)
 (CA INDEX NAME)



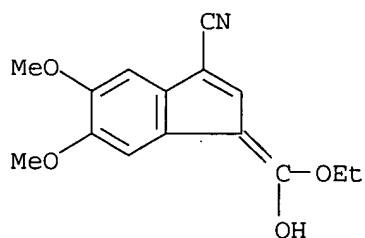
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IT 474024-32-3P 474024-33-4P 474024-34-5P
474024-35-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of 1,5-methano-2,3,4,5- tetrahydro-1H-3-benzazepine via tandem
Michael addition and Pd-catalyzed indene cyclization, hydrogenolysis,
lactam cyclization, and reduction)

RN 474024-32-3 CAPLUS

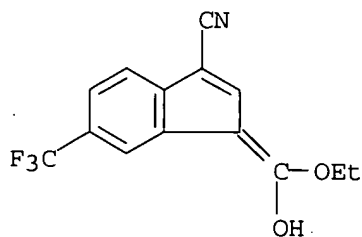
CN 1H-Indene-3-carbonitrile, 1-(ethoxyhydroxymethylene)-5,6-dimethoxy-,
sodium salt (9CI) (CA INDEX NAME)



● Na

RN 474024-33-4 CAPLUS

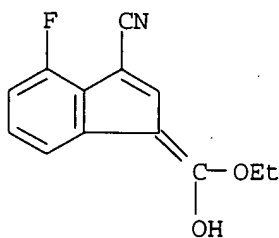
CN 1H-Indene-3-carbonitrile, 1-(ethoxyhydroxymethylene)-6-(trifluoromethyl)-,
sodium salt (9CI) (CA INDEX NAME)



● Na

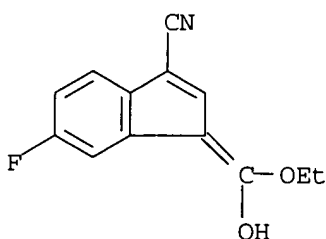
RN 474024-34-5 CAPLUS

CN 1H-Indene-3-carbonitrile, 1-(ethoxyhydroxymethylene)-4-fluoro-, sodium
salt (9CI) (CA INDEX NAME)



● Na

RN 474024-35-6 CAPLUS
 CN 1H-Indene-3-carbonitrile, 1-(ethoxyhydroxymethylene)-6-fluoro-, sodium salt (9CI) (CA INDEX NAME)



● Na

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2002:832750 CAPLUS
 DOCUMENT NUMBER: 137:337794
 TITLE: Process for the preparation of 1,3-substituted indenenes and aryl-fused azapolycyclic compounds
 INVENTOR(S): Singer, Robert Alan; McKinley, Jason Daniel
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA
 SOURCE: PCT Int. Appl., 96 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

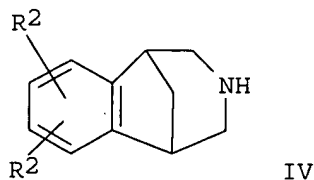
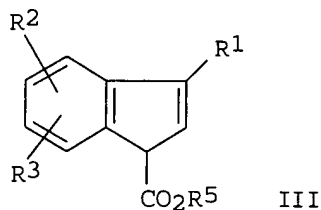
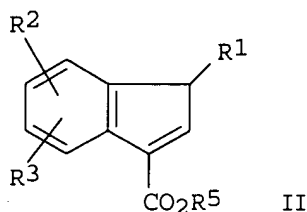
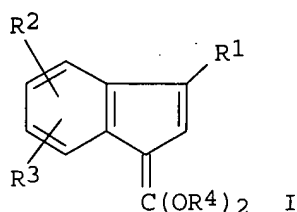
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2002085843 | A2 | 20021031 | WO 2002-IB660 | 20020304 |
| WO 2002085843 | A3 | 20030605 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, | | | | |

GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|--|----|----------|-----------------|------------|
| CA 2443946 | AA | 20021031 | CA 2002-2443946 | 20020304 |
| EP 1383733 | A2 | 20040128 | EP 2002-701498 | 20020304 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2002008992 | A | 20040427 | BR 2002-8992 | 20020304 |
| JP 2004527545 | T2 | 20040909 | JP 2002-583371 | 20020304 |
| US 2003060624 | A1 | 20030327 | US 2002-124135 | 20020417 |
| ZA 2003007205 | A | 20040915 | ZA 2003-7205 | 20030915 |
| PRIORITY APPLN. INFO.: | | | US 2001-285131P | P 20010420 |
| | | | WO 2002-1B660 | W 20020304 |

OTHER SOURCE(S): MARPAT 137:337794

GI

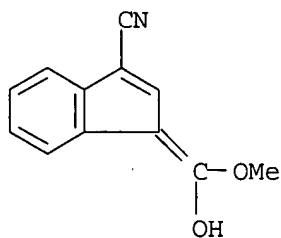


AB The 1,3-substituted indenenes I-III [R1 = CN, alkoxy carbonyl, acyl, aryl, NO2, CF3, sulfonyl; R2, R3 = H, F, Cl, alkylthio, alkylsulfinyl, alkylsulfonyl, (un)substituted NH2, CO2H, CONH2, SO2NH2, alkoxy etc.; R4 = H, ammonium, alkali metal; R5 = alkyl, trialkylsilyl, SiPh3] were prepared as intermediates for the benzoazabicyclooctanones IV which modulate cholinergic function. Thus, 2-BrC6H4C(CN):CHCH2CO2Me which was cyclized to 3-(hydroxymethoxymethylene)-3H-indene-1-carbonitrile sodium salt. Reductive cyclization of the latter compound gave 2,3,4,5-tetrahydro-1,5-methano-1H-benzazepin-2-one.

IT **474024-30-1P 474024-31-2P 474024-40-3P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of 1,3-substituted indenenes as intermediates for aryl-fused azapolycyclic compds. with cholinergic function)

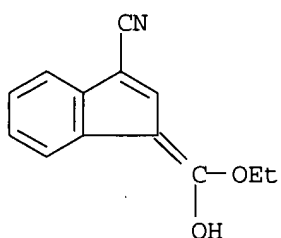
RN 474024-30-1 CAPLUS

CN 1H-Indene-3-carbonitrile, 1-(hydroxymethoxymethylene)-, sodium salt (9CI)
 (CA INDEX NAME)



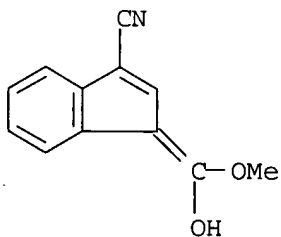
● Na

RN 474024-31-2 CAPLUS
 CN 1H-Indene-3-carbonitrile, 1-(ethoxyhydroxymethylene)-, sodium salt (9CI).
 (CA INDEX NAME)

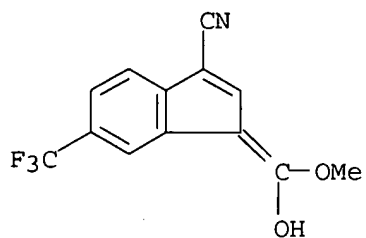


● Na

RN 474024-40-3 CAPLUS
 CN 1H-Indene-3-carbonitrile, 1-(hydroxymethoxymethylene)- (9CI) (CA INDEX NAME)



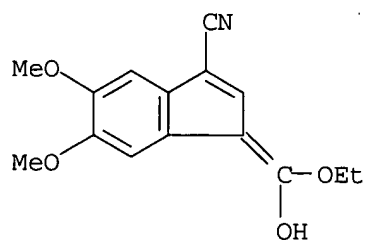
IT 474024-28-7P 474024-32-3P 474024-33-4P
 474024-34-5P 474024-35-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of 1,3-substituted indenenes as intermediates for aryl-fused
 azapolycyclic compds. with cholinergic function)
 RN 474024-28-7 CAPLUS
 CN 1H-Indene-3-carbonitrile, 1-(hydroxymethoxymethylene)-6-(trifluoromethyl)-
 , sodium salt (9CI) (CA INDEX NAME)



● Na

RN 474024-32-3 CAPLUS

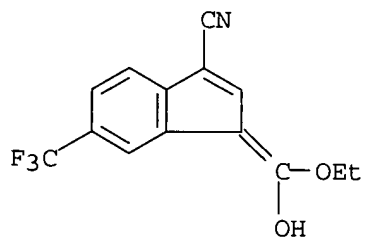
CN 1H-Indene-3-carbonitrile, 1-(ethoxyhydroxymethylene)-5,6-dimethoxy-, sodium salt (9CI) (CA INDEX NAME)



● Na

RN 474024-33-4 CAPLUS

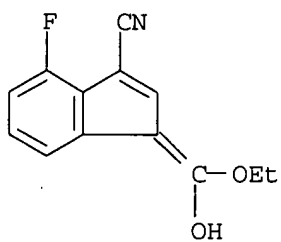
CN 1H-Indene-3-carbonitrile, 1-(ethoxyhydroxymethylene)-6-(trifluoromethyl)-, sodium salt (9CI) (CA INDEX NAME)



● Na

RN 474024-34-5 CAPLUS

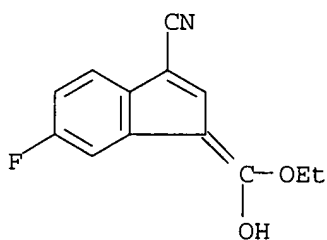
CN 1H-Indene-3-carbonitrile, 1-(ethoxyhydroxymethylene)-4-fluoro-, sodium salt (9CI) (CA INDEX NAME)



● Na

RN 474024-35-6 CAPLUS

CN 1H-Indene-3-carbonitrile, 1-(ethoxyhydroxymethylene)-6-fluoro-, sodium salt (9CI) (CA INDEX NAME)



● Na

=>

4/14/05

STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss full

FULL SEARCH INITIATED 17:24:11 FILE 'CASREACT'

SCREENING COMPLETE - 0 REACTIONS TO VERIFY FROM 0 DOCUMENTS

100.0% DONE 0 VERIFIED 0 HIT RXNS 0 DOCS

SEARCH TIME: 00.00.01

L2 0 SEA SSS FUL L1 (0 REACTIONS)

=> s l1 css full

FULL SEARCH INITIATED 17:24:36 FILE 'CASREACT'

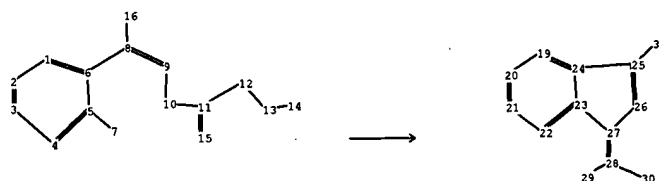
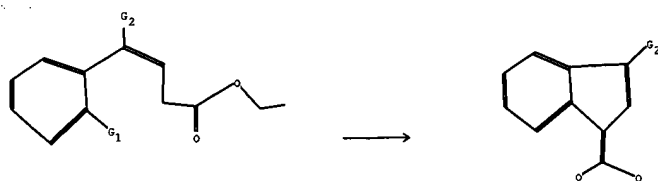
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SEARCH TIME: 00.00.01

L3 0 SEA CSS FUL L1 (0 REACTIONS)

=>



chain nodes :

7 8 9 10 11 12 13 14 15 16 28 29 30 31

ring nodes :

1 2 3 4 5 6 19 20 21 22 23 24 25 26 27

chain bonds :

5-7 6-8 8-9 8-16 9-10 10-11 11-12 11-15 12-13 13-14 25-31 27-28 28-29 28-30

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-24 20-21 21-22 22-23 23-24 23-27 24-25
25-26 26-27

exact/norm bonds :

5-7 8-16 11-12 11-15 12-13 23-27 24-25 25-26 25-31 26-27 28-29 28-30

exact bonds :

6-8 8-9 9-10 10-11 13-14 27-28

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-24 20-21 21-22 22-23 23-24

G1:Cl,Br,F,I

G2:Ph,CO2H,CN,OSO3H,C(O)CH3,NO2

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 19:Atom 20:Atom 21:Atom
22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:CLASS 29:CLASS 30:CLASS
31:CLASS

fragments assigned product role:

containing 19

fragments assigned reactant/reagent role:

containing 1

4/14/05

Uploading C:\Program Files\Stnexp\Queries\indenereact1.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss full

FULL SEARCH INITIATED 17:30:05 FILE 'CASREACT'

SCREENING COMPLETE - 0 REACTIONS TO VERIFY FROM 0 DOCUMENTS

100.0% DONE 0 VERIFIED 0 HIT RXNS 0 DOCS
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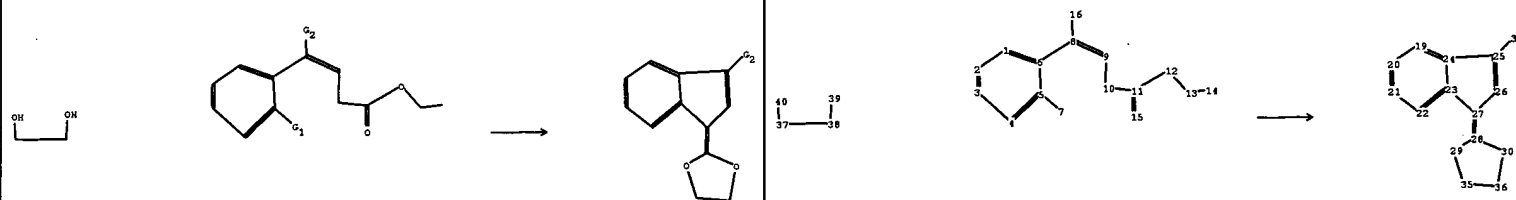
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SEARCH TIME: 00.00.01

L3 0 SEA CSS FUL L1 (0 REACTIONS)

=>



chain nodes :

7 8 9 10 11 12 13 14 15 16 31 37 38 39 40

ring nodes :

1 2 3 4 5 6 19 20 21 22 23 24 25 26 27 28 29 30 35 36

chain bonds :

5-7 6-8 8-9 8-16 9-10 10-11 11-12 11-15 12-13 13-14 25-31 27-28 37-38 37-40
38-39

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-24 20-21 21-22 22-23 23-24 23-27 24-25
25-26 26-27 28-29 28-30 29-35 30-36 35-36

exact/norm bonds :

5-7 8-16 11-12 11-15 12-13 23-27 24-25 25-26 25-31 26-27 28-29 28-30 29-35
30-36 35-36 37-40 38-39

exact bonds :

6-8 8-9 9-10 10-11 13-14 27-28 37-38

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-24 20-21 21-22 22-23 23-24

G1:Cl,Br,F,I

G2:Ph,CO2H,CN,OSO3H,C(O)CH3,NO2

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 19:Atom 20:Atom 21:Atom
22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:CLASS 29:CLASS 30:CLASS
31:CLASS 35:Atom 36:Atom 37:CLASS 38:CLASS 39:CLASS 40:CLASS

fragments assigned reactant role:

containing 37

fragments assigned product role: